Applicants' previous reply. As currently amended, the claim is directed to a cell having, as one of its components, a receptor possessing a transmembrane domain that signals in the absence of an intracellular (rather than an extracellular) signalling moiety, and as another component a CD28 chimeric receptor.

In addition, new claim 101 has been added. This claim finds support throughout the specification, for example, at pages 9 and 48, and in claim 44.

Rejection under 35 U.S.C. § 112, first paragraph

As outlined in the Final Office Action of August 1, 2000, claims 44-47, 51, 52, 72-75, 79, and 100 stand rejected as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that Applicants were in possession of the claimed invention at the time of filing. Specifically, the Examiner states:

> Applicant has no support in the originally filed claims or specification for the genus phrase language "and (c) an intracellular domain that does not signal to said cell to destroy a receptor-bound target cell or receptor-bound target infective agent," present in... claims 44 and 79.

Applicants respectfully traverse this rejection.

The adequate written description requirement of 35 U.S.C. § 112, first paragraph, provides that:

> the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...

The case law makes clear that a specification need not identically describe the claimed subject matter, as seemingly required by the Office in this case. Rather, as stated in *In re Edwards*, 568 F.2d 1349, 196 U.S.P.Q. 465 (C.C.P.A. 1978) (emphasis added):

> To comply with the description requirement it is not necessary that the application describe the claimed invention in *ipsis verbis*, [citation]; all that is required is that it reasonably convey to persons skilled in the art that, as of the filing date thereof, the inventor had possession of the subject matter later claimed by him.

Therefore, in order to meet the written description requirement, Applicants need not utilize any particular form or language of disclosure to describe the subject matter claimed, but "the description must clearly allow persons of ordinary skill in the art to recognize that [applicants] invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989).

This standard has been met in the present case. First, there is no dispute that Applicants have provided a written description in their specification of chimeric receptors that signal target cell or target infective agent destruction through a transmembrane (rather than an intracellular) signalling domain. Indeed, Applicants' claim 44 as originally filed states (emphasis added):

44. A cell expressing a proteinaceous membrane-bound chimeric receptor, said receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) a transmembrane portion derived from a T cell receptor, a B cell receptor, or an Fc receptor which is capable of signalling said cell to destroy a receptor-bound target cell or a receptor-bound target infective agent.

The present claim amendment — which is in dispute — does no more than further clarify that it is the transmembrane, and not the intracellular domain, of the chimera that is responsible for this signalling function.

In truth, support for this clarifying amendment is found in the claims as originally filed. These claims are directed to chimeric receptors that signal host cells to recognize and destroy target cells or target infective agents using a domain specified to be part of the transmembrane moiety.

In addition, however, if there can be any doubt as to whether the application supports this embodiment, that doubt is resolved by looking to the specification, for example, at page 9, lines 16-28. There, Applicants specify that the chimeric immune receptors of the invention may include a transmembrane signalling domain derived from a T cell receptor, Fc receptor, or B cell receptor protein. In addition, at page 48, Applicants specifically describe a transmembrane signalling receptor of the exact sort currently claimed. In particular, at lines 20-33, Applicants detail the construction of a number of chimeras having intracellular domains of reduced length. One such chimera, disclosed at lines 31-33 and in Figure 8A, possesses an intracellular domain of only three amino acid

residues. This intracellular nub does not act as a signalling domain, instead functioning only as an "anchor" that helps to hold the chimera in the cell membrane. As demonstrated in Figure 8B, this receptor, which lacks an intracellular signalling domain, signalled target cell destruction through the transmembrane domain when expressed in cytotoxic T lymphocytes.

In view of Applicants' claims as filed and this specific working example of a chimeric receptor that signals through a transmembrane, rather than an intracellular, domain, there can be no question that Applicants' specification provides a written description that allows persons of skill in the art to recognize that the inventors had possession of the claimed invention at the time of filing. As noted above, the specification need not contain the precise terminology included in the claims; rather, the description must make it clear that Applicants recognized the scope of their invention, as is readily apparent in the present case.

Moreover, the courts have consistently held that "the burden of showing that the claimed invention is not described in the application rests on the PTO... and it is up to the PTO to give reasons why a description not in *ipsis verbis* is insufficient." *In re Edwards* at 1354. The Office, in providing no evidence or reasoning for why Applicants' current description is inadequate, has failed to meet this burden.

For all of the above reasons, Applicants request reconsideration of the § 112, first paragraph rejection and submit that it should be withdrawn.

Information Disclosure Statement

Applicants draw the Examiner's attention to the Information Disclosure Statement mailed September 18, 2000 and request that the Form PTO-1449 submitted with that Statement be initialed and returned with the next action.

Conclusion

Applicants submit that this case is now in condition for allowance, and such action is respectfully requested.

Enclosed is a petition to extend the period for replying for four months, to and including July 31, 2001. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 30 July 2001

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Version With Markings to Show Changes Made

44. (Twice Amended) A cell which expresses at least two proteinaceous membrane-bound chimeric receptors,

the first of said receptors comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, (b) a transmembrane portion derived from a T cell receptor, a B cell receptor, or an Fc receptor protein which, in the absence of an [extracellular] intracellular domain, is capable of signalling said cell to destroy a receptor-bound target cell or a receptor-bound target infective agent, and (c) an intracellular domain that does not signal said cell to destroy a receptor-bound target cell or receptor-bound target infective agent; and

the second of said receptors comprising (a) an extracellular portion which is capable of specifically recognizing and binding said target cell or said target infective agent, and (b) an intracellular portion which is derived from CD28.

51. (Amended) The cell of claim [47] 101, wherein said T cell receptor protein is ζ.

101. (New) The cell of claim 44, wherein said transmembrane portion of the first of said receptors is derived from a T cell receptor protein.